

Successful intravenous thrombolysis of a wake-up stroke with underlying valvular atrial fibrillation

KK Shahedah¹, CS Khoo², WY Wan Nur Nafisah³, CF Ng⁴, I Noor Ashikin⁵, MY Mohd Naim⁶, O Syazarina Sharis⁷, Z Rozman⁸, WZ Wan Asyraf⁹

Abstract

A 42-year-old female admitted with new-onset atrial fibrillation had a wake-up stroke on the high-dependency unit and the time last seen well (TLSW) was 6.5 h. She suffered left-sided body weakness and her National Institutes of Health Stroke Scale (NIHSS) score was 17. An emergency CT perfusion showed right M1 segment occlusion with more than 50% penumbra. She was given recombinant tissue plasminogen activator (r-tPA) at 9 h from TLSW.

An immediate diagnostic angiogram with intention to treat, owing to the presence of large vessel occlusion, showed complete reperfusion after intravenous r-tPA. She was discharged with NIHSS of 2, and at 3-month follow up her Modified Rankin Scale was 0. We demonstrated a successful reperfusion and excellent clinical recovery with intravenous thrombolysis in a patient who presented with a wake-up stroke with underlying valvular atrial fibrillation despite evidence of large vessel occlusion.

Keywords: atrial fibrillation, computed tomography perfusion, r-tPA, wake-up stroke

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Correspondence to:

WZ Wan Asyraf
Medical Department
Pusat Perubatan Universiti
Kebangsaan Malaysia
Kuala Lumpur
Malaysia

Email:

wan.asyraf.wan.zaidi@
ppukm.ukm.edu.my

Introduction

The determination of time of onset is paramount in acute stroke thrombolytic treatment with intravenous recombinant tissue plasminogen activator (r-tPA), which was approved in 1996 by Food and Drug Administration; however, we cannot accurately determine the time of onset if a patient wakes with the stroke symptoms. This is called 'wake-up stroke' (WUS).¹ Approximately 20% of stroke patients present with WUS, and the odds of detecting new atrial fibrillation (AF) are three-fold higher in WUS patients.² Administration of intravenous r-tPA treatment in this patient group has yet to be incorporated into guidelines owing to lack of high-level evidence. Despite the recent breakthrough of endovascular thrombectomy from the DAWN and DEFUSE-3 trials, which also recruited WUS patients, endovascular treatment is not widely available and too expensive.^{3,4} In our patient, who presented with WUS, intravenous thrombolysis guided by CT perfusion findings resulted in successful reperfusion despite evidence of M1 occlusion.

Case

A 42-year-old female was found to have new-onset fast AF and was observed in the high-dependency ward. She later

woke-up with a stroke, and the time last seen well (TLSW) was approximately 6.5 h prior to referral to the stroke team. Clinically, her blood pressure was 160/100 mmHg with heart rate of 90 beats per minute. She suffered left-sided hemiplegia with ipsilateral facial weakness and left-sided hemi-neglect. The National Institutes of Health Stroke Scale (NIHSS) was 17. An emergency CT perfusion showed right M1 segment occlusion and the Alberta Stroke Program Early CT score (ASPECTS) was 8, with >50% penumbra. She was given r-tPA (0.9 mg/kg) at 9 h from TLSW, and the digital subtraction angiogram, with intention to treat due to presence of large vessel occlusion, showed successful reperfusion [thrombolysis in cerebral infarction (TICI) score of 3] after intravenous thrombolysis; therefore, thrombectomy was not required. The NIHSS improved to 2 upon discharge, and warfarin was started on day 12 from onset. Three months later, her Modified Rankin Scale was 0. Transoesophageal echocardiogram revealed she suffered moderate-to-severe mitral stenosis with evidence of a planimetered mitral valve area of <1 cm². Both mitral valve leaflets tips were noted to be thickened, with severely restricted mobility. Dilated left atrium with good systolic function was seen. Left atrial appendage was also noted to be dilated and with reduced exit velocity. There was

¹Clinical Neurologist and Lecturer, Neurology Unit, Department of Internal Medicine, International Islamic University Malaysia, Kuantan, Pahang, Malaysia; ^{2,4,9}Clinical Neurologist and Lecturer, ³Consultant of Internal Medicine & Neurology and Senior Lecturer, ⁵Senior Registrar of Internal Medicine, Department of Medicine, Pusat Perubatan Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia; ⁶Senior Registrar of Radiology, ⁷Consultant Radiologist, ⁸Consultant Interventional Radiologist, Department of Radiology, Pusat Perubatan Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia

Figure 1 Plain head CT. Red arrow shows dense right middle cerebral artery sign

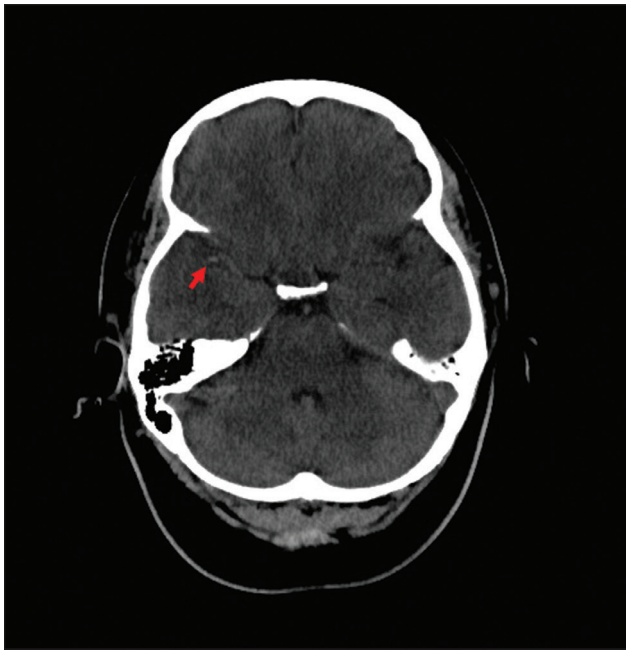
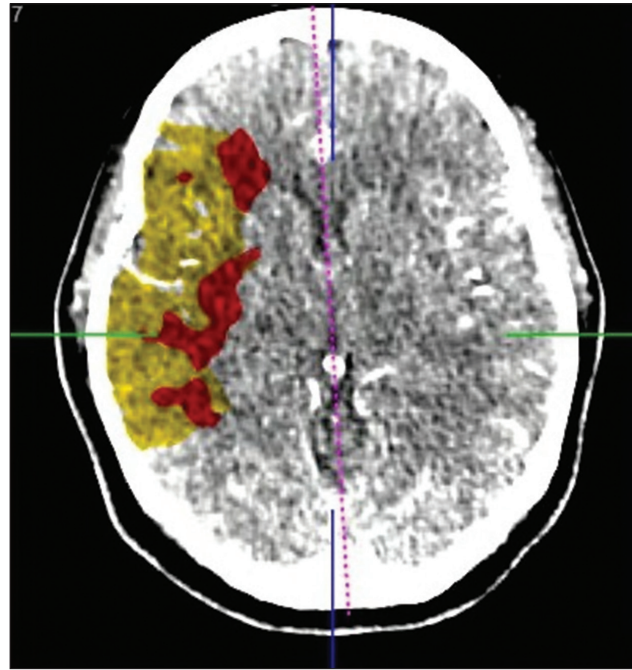


Figure 2 Head CT with perfusion showing significant penumbra area



evidence of spontaneous echo contrast over the left atrium and left atrial appendage; however, no definite thrombus was seen. There was no evidence of patent foramen ovale or septal defect. The patient was later scheduled for valve replacement (Figures 1–3).

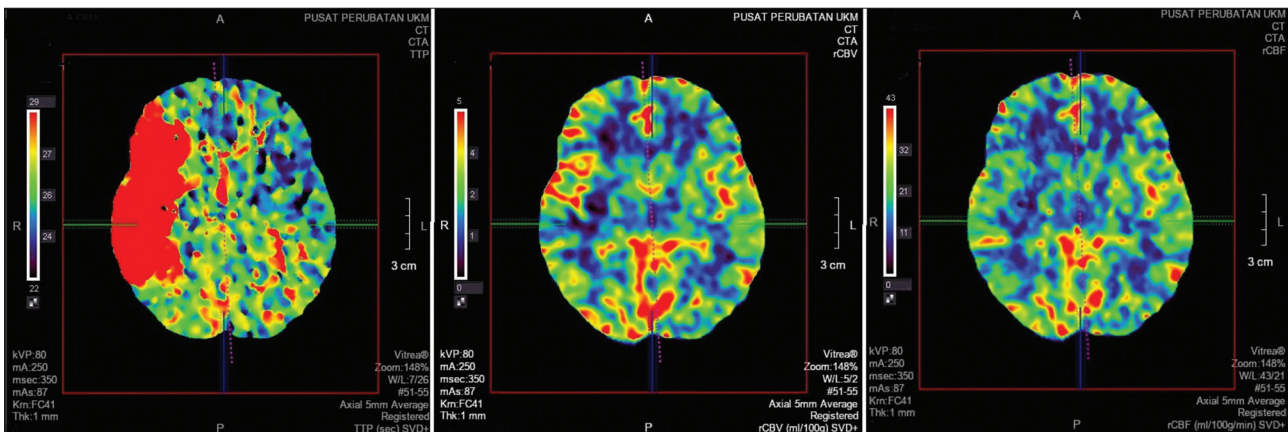
Discussion

AF is one of the major risk factors for ischemic stroke, and is associated with a four-fold increased risk of stroke. AF patients suffer cardio-embolic stroke due to thrombus formation at the left atrial appendage. The presence of AF is associated with high 30-day and 1-year case-mortality rate and higher stroke recurrence rate within the first year of follow up, as well as poorer survival after an average follow up of 45 months.⁵ Therefore, stroke patients with AF have a poorer neurological outcome than patients with no

AF.⁶ Furthermore, the association of AF with WUS has been established, with the odds of detecting a newly diagnosed AF three-fold higher among WUS patients.²

To date, thrombolytic treatment is considered ‘off-label’ for patients presenting with WUS. After publication of ECASS-3 study the r-tPA treatment window has been extended to 4.5 h from onset.⁷ The advancement of radiology modalities, including MRI and CT perfusion, allow neurologists to evaluate the salvageable area called ‘penumbra’. Reperfusion therapy would be able to rescue this ischemic area before it is infarcted; however, most of the recently published randomised controlled trials (RCTs) utilised these modalities to assist in the decision-making prior to endovascular intervention, with the treatment window extended to within 16–24 h.^{3,4} We are still waiting for the ongoing RCT looking into the extending time window

Figure 3 The time to peak, cerebral blood volume and cerebral blood flow of CT perfusion images showed more than 50% penumbra with small infarct core



for thrombolytic treatment in acute ischemic stroke, which will be more feasible to a significant number of patients, especially those in developing countries.⁸ As in our case, the endovascular treatment is not readily available and too expensive for the patient. We believe early thrombolytic treatment is a cost-effective intervention even though there is evidence of large vessel occlusion.

Recent meta-analysis published in January 2018 showed 11% of patients who received intravenous r-tPA managed to obtain successful reperfusion without endovascular treatment. The number of patients with r-tPA-induced successful reperfusion increased to 17% if the study excluded patients who presented with tandem lesions.⁹ Our patient suffered a cardio-embolic stroke due to underlying valvular AF, which explained the severity of the stroke; however, the prompt treatment provided to her resulted in a successful treatment outcome radiologically, and most importantly, immediate clinical improvement.

Conclusion

This is the first case report in Malaysia related to successful reperfusion with r-tPA in WUS. CT perfusion-guided thrombolysis in WUS is safe and cost effective, especially in developing countries. Our case illustrated successful thrombolysis of acute M1 occlusion guided by CT perfusion, which resulted in immediate recovery and reduced long-term morbidity associated with cardio-embolic stroke. Larger clinical data are needed to look at the safety and efficacy of extending the time window for thrombolysis, especially if endovascular interventions are not feasible. ①

Informed consent

Written informed consent for the paper to be published (including images, case history and data) was obtained from the patient for publication of this paper, including accompanying images.

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